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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,616	11/15/2000	Hidetoshi Inoko	06501-069001/ C1-X0011-US	3868

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EXAMINER

EINSMANN, JULIET CAROLINE

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 06/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/713,616

Applicant(s)

INOKO ET AL.

Examiner

Juliet Einsmann

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) 5-9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 14,16.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1, particularly SEQ ID NO: 1 and 2 in Paper No. 13 is acknowledged. The traversal is on the ground(s) that all of the microsatellite markers are located in the human MHC class II region, and thus, examining these claims together would present no undue burden on the examiner. It is noted that Applicant refers to the further restriction requirement regarding sequences as a "species election." However, it is noted that this is not a species election but a further restriction, as stated in the requirement. Nonetheless, Applicant requests the recombination of groups I and II and that the further restriction regarding sequences be withdrawn. Thus, there are two separate issues in the traversal. Applicant's arguments concerning the separation of groups I and II are not persuasive because these groups are separately classified, and the separate classification of groups I and II is *prima facie* evidence that the examination of these inventions would place an undue burden on the examiner. Applicant has not provided an evidence or arguments to overcome this burden. Applicant's only argument, that each of the microsatellite markers of the present invention are in the MHC class II region is not persuasive because it does not address the distinct subject matter being claimed in groups I and II. Furthermore, the searches required to examine the instantly claimed methods and the instantly claimed probes would be different, requiring a search of different classes, different electronic databases and the use of different key words in such a search.

In addition, Applicant's argument that all of the microsatellite markers are in the MHC class II region and thus would not pose a substantial burden for examination is also not persuasive. The MHC class II region spans over approximately 1.1 Mb and contains more than

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30 functional genes (see specification, page 2). Thus, the fact that each of these distinct polymorphisms, and the sequences that flank them are in the MHC class II region does not remove the burden required to examine each particular marker and sequence. The markers themselves and the primers that would amplify them are distinct from one another, having different structures. A search of one marker or primer would not suggest another. Each sequence, therefore, requires a separate search of the literature.

For these reasons, the requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 are indefinite over the recitation of "capable of specifically hybridizing" because capability is a latent characteristic and the claims do not set forth the criteria by which to determine capability. That is, it is not clear whether the recited probes have the potential to hybridize or do in fact hybridize a DNA having the sequence of the flanking regions of a microsatellite. Amendment of the claim to read, for example, "which specifically hybridizes" would obviate this rejection.

Claims 1-2 are further indefinite over the meaning of "specifically hybridizing" because it is not clear what limitation this phrase imparts on the claimed primers. The specification, at

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page 9, teaches that "specifically hybridizing" means that there is no significant cross-hybridization to unrelated regions of the genome under ordinary hybridization conditions, and preferably under high stringency conditions." However, one of the elected embodiments, SEQ ID NO: 2, exhibits full sequence identity with sequences other than the claimed sequence (see 103 rejections). This sequence, therefore, would cross-hybridize with each of these sequences in which it is contained. Thus, the meaning of the phrase "specifically hybridizing" is unclear.

Claims 1-4 refer to "the sequence" of "the flanking regions" of a microsatellite, however these particular phrases lack proper antecedent basis in the claims. Thus, it is not clear to which sequence or regions these phrases refer. Particularly it is not clear what it means for a primer to have "the sequence of the flanking regions" in light of the fact that these regions are undefined in the claims.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that these claims currently contain non-elected subject matter, this rejection is directed only to the elected microsatellite, M2_4_9.

The rejected claims are drawn to an oligonucleotide primer that is capable of specifically hybridizing to a DNA having the sequence of the flanking regions of the microsatellite M2_4_9, and a kit that comprises a pair of oligonucleotide primers having the sequence of the flanking regions of said microsatellite. The specification teaches that the "flanking region" of a microsatellite can be several thousands of bases (page 8). Thus, the genus of these claimed primers comprises millions of possibilities.

For M2_4_9, the specification has provided two such primers, SEQ ID NO: 1 and 2. Thus, applicant has express possession of only one species in a genus which comprises hundreds of millions of different possibilities. The specification has not described any additional flanking sequences. These sequences are essential subject matter for the practice of this invention. The specification teaches, in table 2, page 18, that the elected microsatellite sequence is between the genes ARE1 and RING1, indicating that this flanking region is at least 38,000 base pairs. The specification, however, fails to describe this "flanking region" in any more detail. No sequence structure is given from which to select the claimed primer or primer pair, beyond the disclosure of SEQ ID NO: 1 and SEQ ID NO: 2.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the instant application, only the nucleic acid sequence of the disclosed SEQ ID Nos are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

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"...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description of any primers that meet the limitations of claims 1 and 3, other than the two specific sequences that are disclosed.

Claim Rejections - 35 USC § 101

6. Claims 1-4 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

Claims 1-4 are drawn to primers that hybridize to regions that flank recited microsatellite polymorphic regions. These primers are capable of amplifying the microsatellite polymorphic regions disclosed in the specification, particularly elected microsatellite M2_4_9. The specification asserts that "these novel polymorphic microsatellites will provide useful genetic markers in HLA related research, such as genetic mapping of HLA class II associated diseases, transplantation matching, population genetics, and identification of recombination hot spots as well as linkage (page 4)." However, none of these asserted utilities are specific to the particular polymorphic satellites disclosed herein. These utilities are general to an entire class of nucleic acids, that is any nucleic acid that is a microsatellite or that has a polymorphism. Applicant selected these particular polymorphisms based on a computer screen of a large region of nucleic acid, and then further selected specific polymorphic regions (of which M2_4_9 is one) because they have a large number of alleles. However, simple selecting nucleic acids that have a particular characteristic that does not have an associated specific utility for the characteristic does not provide a specific associated utility. The specification has not disclosed any particular

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features of the claimed primers to amplify polymorphic regions that imparts a specific utility for the claimed primers.

Claims 1-4 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by 1997 Boehringer Mannheim Biochemicals Catalog, page 95.

Boehringer Mannheim provide a mixture of hexamer nucleotides of all possible sequences for random primed DNA labeling (Catalog number 1277081). These primers would be “capable of specifically hybridizing to a DNA having the sequence of the flanking regions of” M2_4_9, wherein “specifically hybridizing” is understood to be a hybridization event wherein base pair matching occurs between the primer and the target sequence. These primers further have portions of “the sequence of the flanking regions” of a microsatellite because they represent all possible hexamer sequences.

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9. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Zavada *et al.* (US 5955075).

Zavada *et al.* teach an oligonucleotide that is capable of specifically hybridizing to a DNA having the flanking sequence of the microsatellite M2_4_9. Nucleic acid SEQ ID NO: 63 taught by Zavada *et al.* comprises instant SEQ ID NO: 2 (see nucleotides 73-92 of the Zavada *et al.* sequence). With regard to the limitation that the claimed oligonucleotide be a "primer" this is considered a statement of intended use. In the instant case, the oligonucleotide taught by Zavada *et al.* would be capable of acting as a primer because it has an extendable 3' end.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-2 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Zavada et al.* (US 5955075) in view of Wu (US 5387510).

Zavada et al. teach a nucleic acid sequence that comprises instant SEQ ID NO: 2 (see nucleotides 73-92 of the *Zavada et al.* sequence). *Zavada et al.* do not teach a primer that is SEQ ID NO: 2.

Wu teach methods for the detection of target sequence that utilize probes of fifteen to twenty nucleotides in length (Col. 2, for example).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have selected an oligonucleotide probe from the sequence taught by *Zavada et al.* for use in the methods taught by Wu. The ordinary practitioner would have been motivated to use the method taught by Wu because Wu teaches that their method provides "a means for rapid and sensitive detection of nucleic acids (Col. 3, lines 28-30)." Furthermore, the ordinary practitioner would have been motivated to select probes of twenty nucleotides in length because Wu teaches that "the oligonucleotide of the probes is of a critical length, that is from 15 to 20 nucleotides (Col. 1)." Thus, the selection of a probe consisting of SEQ ID NO: 2 is *prima facie* obvious in view of the teachings of *Zavada et al.* in view of Wu. With regard to the limitation that the claimed oligonucleotide be a "primer" this is considered a statement of intended use. In the instant case, the oligonucleotide taught by *Zavada et al.* in view of Wu would be capable of acting as a primer because it has an extendable 3' end.

Conclusion

13. No claims are allowed. Claim 4, restricted to the elected sequences (SEQ ID NO: 1 and SEQ ID NO: 2) is free of the prior art.

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14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Juliet C. Einsmann
Examiner
Art Unit 1634

May 16, 2002



W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600